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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,204	05/11/2001	Peter Martin Fischer	CCI-010DV	8487

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/854,204	Fischer et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 47, and 49-71* is/are pending in the application.

4a) Of the above, claim(s) *67-71* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 47, and 49-66* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicant election of the species of SEQ ID NO:2.

2. Claim 1 has been amended. Claim 48 has been canceled. Claims 1, 47 and 49-71 are examined on the merits.

Specification

The specification is objected to for stating that the instant application is a divisional of application 09/438,460. The restriction in 09/438,460 was as follows:

I. Claims 1-18 and 45, drawn to carrier peptides consisting of SEQ ID NO:1 and variants thereof, classified in class 514, subclass 2.

II. Claims 19-21, 28-38, 43 and 44, drawn to a membrane translocation vector comprising SEQ ID NO:1 linked to a polynucleotide, classified in class 514, subclass 2 and class 514, subclass 44. Claims 19-21, 28-38, 43 and 44 will be examined with this group to the extent that the claims read on polynucleotides.

III. Claims 19, 20, 22, 23, 28-38 and 39-44, drawn to a membrane translocation vector comprising SEQ ID NO:1 linked to a polypeptide, classified in class 514, subclass 2. Claims 19, 20, 28-38, 43 and 44 will be examined with this group to the extent that the claims read on polypeptides.

IV. Claims 19, 20, 24-38, 43, 44 and 46, drawn to a membrane translocation vector comprising SEQ ID NO:1 linked to a non-polypeptide, non-polynucleotide drug, classified in class 514, subclass 2. Claims 19, 20, 28-38, 43 and 44 will be examined with this group to the extent that the claims read on non-polypeptide, non-polynucleotide drugs.

The examined invention of 09/438,460 was Group I, drawn to carrier peptides consisting of SEQ ID NO:1 and variants thereof. It appears that the instant claims 1, 47 and 49-71 are also drawn to carrier peptides alone as the claims do not encompass the peptides conjugated or fused to

polynucleotides, heterologous polypeptides or non-peptide drugs. Thus, the instant application is a continuation, rather than a divisional of 09/438,460.

Claim Objections

3. Claims 52 and 53 are objected to for depending on claim 48 which has been canceled.

4. Claims 67-71 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim, such as claims 67 or 68, cannot be dependent upon another multiply dependent claim such as claims 53 or 52, respectively. See MPEP § 608.01(n). Accordingly, claims 67 and 68 and dependent claims 69-71 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

5.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 47, 50, 52, 53, 54, 60-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear how the recitation of the assignment of amino acids in claim 52 further defines any of claim 47 and 49-51 as the amino acids have already been defined by the specification on page 6, line 29 to page 7, line 2 and are in agreement with that recognized in the art. Further, it is unclear how the recitation of "basic for basic" etc in claim 50 further defines claim 49 which incorporates the specific limitation of "homologous" replacement.

Claim 53 recites "such as trifluorotyrosine*" and "such as 4-methyl-Phe*" The phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 47, 54, 61, 64 and 65 refer to amino acid residues which are "reversed". It is unclear whether this reversal refers to the linkage of the amino acid to the peptide backbone, or if the reversal refers to the position of the amino acid within the amino acid sequence.

Claims 60-66 refer to positions 1-6 of the carrier moiety of claim 1. However, it is unclear what these positions correspond to, as claim 1 is drawn in part to variants of SEQ ID NO:2 which could incorporate or delete amino acids from SEQ ID NO:2.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 47, and 49-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a genus of peptides comprising variants of SEQ ID NO:2. The specification states on page 6, lines 1-5: the specific amino acid residues of the peptide may be modified in such a manner that retains there ability to translocate; such modified peptides are referred to as "variants". It is noted that the type of translocation is not defined as part of the limitation of a variant. It is known in the art that molecules can translocate from the extracellular environment through the plasma membrane to the intracellular environment, or can translocate from the intracellular environment of the golgi complex to the extracellular environment via secretory mechanisms, or peptides and proteins can translocate from the cytoplasm through the mitochondrial or nuclear membranes (see for example, Stratford et al, WO 99/45127, page 17, line 16, page 20, line 15, page 27, line 17). The specification teaches the peptides of SEQ ID NO:1-19 as having the ability to penetrate the

plasma membrane from the external environment. The claims are drawn to variants of these SEQ ID NO that have the ability to generally translocate. The specification lacks teachings regarding the distinguishing attributes of peptides which can translocate from the intracellular environment to the extracellular environment, or the distinguishing attributes of peptides which can translocate from the cytoplasm into the nucleus or mitochondria. The specific or claims do not place any limit on the number of amino acid substitutions, deletions, insertions and or additions that may be made to SEQ ID NO:2. Thus the scope of the claims is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to provide common attributes or characteristics that identify members of the genus, ad because the genus is highly variant, encompassing peptides having numerous properties of translocation, SEQ ID NO:1-19 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe all possible translocating proteins. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 1, 47, 49, 50, 51, 52, 60, 61, 62, 64, 65 and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Chassaing et al (WO 97/12912). Claim 1 is drawn in part to variants of the membrane translocation peptide carrier moiety of SEQ ID NO:2. Claim 47 embodies the carrier moiety of claim 1 wherein one or more amino acid residues are replaced by naturally-occurring or non-naturally occurring amino acid residues. Claim 49 embodies the carrier moiety of claim 1 wherein one or more amino acids are replaced by homologous replacement. Claim 50 specifies that homologous replacement is basic for basic, acidic for acidic, etc. Claim 51 embodies the carrier moiety of claim 1 wherein one or more amino acids are replaced by non-homologous replacement. Claim 52 recites the definitions for basic, acidic, non-polar and polar amino acids. Claim 60 embodies the carrier moiety of claim 1 wherein one or more amino acid residues at positions 1, 2, 3, 5 or 6 are replaced by naturally or non-naturally occurring amino acids. Claim 62 embodies the carrier moiety of claim 1 wherein the amino acid residue at positions 3 or 7 is replaced. Claim 63 specifies that the amino acid residue at position 3 is replaced. Claim 66 is drawn to the carrier moiety of claims 49 or 50 wherein the homologous replacement occurs at any of positions 1 and 2.

Chassaing et al disclose the peptide of Tables I and II, wherein the peptides 43-58, 58-43, 43-58 (D), pro50, 3pro and 41-55 are able to carry biotin as a cargo moiety into a cell (figure 5A and B, page 11, lie 30 to page 12, line 8). The peptide 43-58 comprises SEQ ID NO:2 and is therefore a variant of SEQ ID NO:2 as it has conserved the functional activity of translocation. Chassaing et al disclose that the amino acid residues can b replaced by (D) amino acids, thus fulfilling the specific embodiment of claim 60 and claim 47 drawn to non-naturally occurring amino acids. Chassaing et al disclose the same definitions for acidic, basic, polar and non-polar amino acids as claim 52 (page 4, lines 3-13). Chassaing et al disclose homologous substitutions at

positions 3, 7 and 14 (page 5, lines 18-22), thus fulfilling the specific embodiments of claims 60, 62 and 63. Chassaing et al disclose that the Met-Arg peptide can translocate biotin into a cell. The Met-Arg peptide results from the substitution of Met for Arg in position 1 of the instant SEQ ID NO:2 and the substitution of Arg for Met at position 3 of SEQ ID NO:2, thus fulfilling the specific embodiment of claim 51 drawn to non-homologous replacement. Chassaing et al also disclose that the retro-inverso sequence of 43-58 (58-43) also retains the ability to translocate biotin into a cell, thus fulfilling the specific embodiment of claim 47 part b, claim 54 and claims 61, 64 and 65 since the entire amino acid sequence, as well as the linkages between the amino acid residues, was reversed (page 3, lined 10-11 figure 5A and B). Further the 58-43 sequence as compared to the 43-58 sequence has a homologous replacement of Lys for Arg in position 1, fulfilling the specific limitation of claim 66.

11. Claims 1, 47, 49- 53, 59 and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Nadler et al (U.S. 5,877,282). The embodiments of claims 1, 47, 49-52 and 60 are recited above. Claim 53 is drawn in part to the carrier moiety of according to any of claims 47 to 51, wherein the replacement amino acid is alpha substituted amino acids, N-alkyl amino acids, halide derivative of natural amino acids or methyl derivatives of Phe. Claim 59 embodies the carrier moiety of claim 1 wherein one or more amino acids are in peptoid form.

Nadler et al disclose that carrier moieties such as the antennapedia homeodomain, FGF, HIV, TAT or Hsc70 and derivative or mimetics thereof are capable of delivering a cargo moiety through the cytoplasmic membrane into a cell (column 8, lines 9-20). As claim 1 does not limit the number of animo acid substitutions or deletions that can be encompassed by a variant, all of the antennapedia homeodomain, FGF, HIV, TAT or Hsc70 can be considered as variants of SEQ ID NO:2. Nadler et al also disclose the incorporation of D amino acids into the peptide sequence fulfilling the specific embodiments of claim 60 and claim 47 drawn to non-naturally occurring amino acids (column 6, lines 3-7). Nadler et al defines a derivative of a peptide as a homologous

polypeptide in which conservative or non-conservative substitutions have been made resulting in a peptide which retains its translocation function (column 6, lines 8-14), thus fulfilling the specific embodiment of claims 49-52. Nadler et al disclose peptoid amino acids, N-substituted, especially t-butyl substituted amino acids and fluorenylmethoxy-carbonyl alpha amines (column 12, lines 36-52).

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

14. Claims 1, 47, and 49-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 11-18 and 45 of copending Application No. 09/438,460. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant carrier moieties can be anticipated by the carrier moiety species of the '460 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
February 21, 2003